

69. (Amended) A synthetic nucleic acid sequence which encodes a human protein wherein at least one non-common codon or less-common codon has been replaced by a common codon encoding the same amino acid residue as the non-common or less-common codon, and the synthetic nucleic acid sequence comprises a continuous stretch of common codons, which continuous stretch includes at least 60% or more of the codons in the synthetic nucleic acid sequence, wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B.

73. (Amended) A synthetic nucleic acid sequence which encodes a human protein wherein at least one non-common codon or less-common codon has been replaced by a common codon encoding the same amino acid residue as the non-common or less-common codon, and wherein at least 98% or more of the codons in the sequence encoding the protein are common codons and wherein the protein is at least 90 amino acid residues in length, wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B.

81. (Amended) A synthetic nucleic acid sequence which encodes human Factor VIII or a functional portion thereof, wherein at least one non-common codon or less-common codon has been replaced by a common codon encoding the same amino acid residue as the non-common or less-common codon and wherein the synthetic nucleic acid has a continuous stretch of at least 150 codons all of which are common codons, wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B.

85. (Amended) A synthetic nucleic acid sequence which encodes human Factor VIII or a functional portion thereof, wherein at least one non-common codon or less-common codon has been replaced by a common codon encoding the same amino acid residue as the non-common or

wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B.

89. (Amended) A synthetic nucleic acid sequence which encodes human Factor VIII or a functional portion thereof, wherein at least one non-common codon or less-common codon has been replaced by a common codon encoding the same amino acid residue as the non-common or less-common codon and wherein at least 98% or more of the codons in the sequence encoding the Factor VIII are common codons and the Factor VIII is at least 90 amino acid residues in length, and wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B.

97. (Amended) A synthetic nucleic acid sequence which encodes human Factor IX, wherein at least one non-common codon or less-common codon has been replaced by a common codon encoding the same amino acid residue as the non-common or less-common codon and wherein the synthetic nucleic acid has a continuous stretch of at least 150 codons all of which are common codons, and wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B.

100. (Amended) A synthetic nucleic acid sequence which encodes human Factor IX, wherein at least one non-common codon or less-common codon has been replaced by a common codon encoding the same amino acid residue as the non-common or less-common codon and wherein the synthetic nucleic acid has a continuous stretch of common codons which comprise at least 60% of the codons of the synthetic nucleic acid sequence, and wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B.

103. (Amended) A synthetic nucleic acid sequence which encodes human Factor IX,

wherein at least one non-common codon or less-common codon has been replaced by a common codon encoding the same amino acid residue as the non-common or less-common codon and wherein the synthetic nucleic acid has a continuous stretch of common codons which comprise at least 60% of the codons of the synthetic nucleic acid sequence, and wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B.

6-10
excluded

codons and the Factor IX is at least 90 amino acid residues in length, and wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B.

113. (Amended) A synthetic nucleic acid sequence which encodes a human protein wherein at least one non-common codon or less-common codon has been replaced by a common codon encoding the same amino acid residue as the non-common or less-common codon, wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B and having the following properties:

(i) the synthetic nucleic acid sequence comprises a continuous stretch of at least 150 codons all of which are common codons;

(ii) the synthetic nucleic acid sequence comprises a continuous stretch of common codons, which continuous stretch includes at least 60% or more of the codons in the synthetic nucleic acid sequence; and

(iii) wherein at least 98% or more of the codons in the sequence encoding the protein are common codons and wherein the protein is at least 90 amino acid residues in length.

114. (Amended) A method for preparing a synthetic nucleic acid sequence which is at least 90 codons in length, comprising:

identifying a non-common codon and a less-common codon in a non-optimized gene sequence which encodes a human protein and is at least 90 codons in length; and

replacing at least 98% of the non-common and less-common codons with a common codon encoding the same amino acid residue as the replaced codon, wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B.

synthesizing at least two fragments of a nucleic acid sequence, wherein the two fragments encode contiguous portions of a human protein of at least 90 amino acids and wherein both fragments are mRNA optimized; and

joining the two fragments to create a nucleic acid encoding the human protein, such that a non-common codon is not created at a junction point, thereby making the mRNA optimized nucleic acid sequence.

119. (Amended) A method for preparing a synthetic nucleic acid sequence encoding a human protein which is at least 90 amino acid residues in length, comprising identifying non-common codon and less-common codons in the non-optimized nucleic acid sequence encoding a protein of at least 90 amino acid residues in length and replacing at least 98% or more of the non-common and less-common codons of the nucleic acid sequence encoding the protein with a common codon encoding the same amino acid residue as the replaced codon, wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B, thereby preparing a synthetic nucleic acid sequence encoding a human protein which is at least 90 amino acid residues in length.

120. (Amended) A primary or secondary mammalian cell having an exogenous synthetic nucleic acid sequence which encodes a human protein or a polypeptide wherein at least one non-common codon or less-common codon has been replaced by a common codon encoding the same amino acid residue as the non-common or less-common codon, wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B, and wherein the synthetic nucleic acid has a continuous stretch of at least 150 codons all of which are common codons; is at least 80 base pairs in length; and is free of unique restriction endonuclease sites in the message optimized sequence; and has

DNA sequences, sufficient for expression of the exogenous synthetic DNA in the transfected primary or secondary cell.

125. (Amended) A primary or secondary mammalian cell having an exogenous synthetic nucleic acid sequence which encodes a human protein or a polypeptide wherein at least one non-common codon or less-common codon has been replaced by a common codon encoding the same amino acid residue as the non-common or less-common codon, wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B, and wherein the synthetic nucleic acid has a continuous stretch of common codons which comprise at least 60% of the codons of the synthetic nucleic acid sequence, is at least 80 base pairs in length and is free of unique restriction endonuclease sites in the message optimized sequence; and has

DNA sequences, sufficient for expression of the exogenous synthetic DNA in the transfected primary or secondary cell;

the primary or secondary cell capable of expressing the human protein or polypeptide product.

130. (Amended) A primary or secondary mammalian cell having an exogenous synthetic nucleic acid sequence which encodes a human protein or a polypeptide wherein at least one non-common codon or less-common codon has been replaced by a common codon encoding the same amino acid residue as the non-common or less-common codon, wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B, and wherein at least 98% or more of the codons in the sequence encoding the protein are common codons and the protein is at least 90 amino acids in length; the nucleic acid sequence is at least 80 base pairs in length and is free of unique restriction endonuclease sites in the message optimized sequence; and has

DNA sequences, sufficient for expression of the exogenous synthetic DNA in the transfected primary or secondary cell;

the primary or secondary cell capable of expressing the human protein or polypeptide product

135. (Amended) A primary or secondary mammalian cell having an exogenous synthetic nucleic acid sequence which encodes a human protein or a polypeptide wherein at least one non-common codon or less-common codon has been replaced by a common codon encoding the same amino acid residue as the non-common or less-common codon, wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B, and wherein the synthetic nucleic acid has the following properties: it has a continuous stretch of at least 150 codons all of which are common codons; it has a continuous stretch of common codons which comprise at least 60% of the codons of the synthetic nucleic acid sequence; at least 98% or more of the codons in the sequence encoding the protein are common codons and the protein is at least 90 amino acids in length; it is at least 80 base pairs in length and which is free of unique restriction endonuclease sites in the message optimized sequence; and

DNA sequences, sufficient for expression of the exogenous synthetic DNA in the transfected primary or secondary cell;

the primary or secondary cell capable of expressing the human protein or polypeptide product.

In the drawings:

Please add the 2 enclosed drawing sheets (Fig. 14A-B) to the application.